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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/248,158	02/09/1999	ZHENGYU YUAN	342312000600	8469

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1639

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/248,158</b>	Applicant(s) <b>Yuan et al.</b>						
	Examiner <b>Maurie G. Baker, Ph.D.</b>	Art Unit <b>1639</b>						
								
<b>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</b>								
<b>Period for Reply</b> <p>A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>THREE</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.</p> <ul style="list-style-type: none"> <li>- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.</li> <li>- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.</li> <li>- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.</li> <li>- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).</li> <li>- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).</li> </ul>								
<b>Status</b> <p>1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Feb 14, 2003</u></p> <p>2a) <input checked="" type="checkbox"/> This action is FINAL.      2b) <input type="checkbox"/> This action is non-final.</p> <p>3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i>, 1935 C.D. 11; 453 O.G. 213.</p>								
<b>Disposition of Claims</b> <p>4) <input checked="" type="checkbox"/> Claim(s) <u>1, 3, and 5-20</u> is/are pending in the application.</p> <p>4a) Of the above, claim(s) <u>11-18 and 20</u> is/are withdrawn from consideration.</p> <p>5) <input type="checkbox"/> Claim(s) _____ is/are allowed.</p> <p>6) <input checked="" type="checkbox"/> Claim(s) <u>1, 3, 5-10, and 19</u> is/are rejected.</p> <p>7) <input type="checkbox"/> Claim(s) _____ is/are objected to.</p> <p>8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.</p>								
<b>Application Papers</b> <p>9) <input type="checkbox"/> The specification is objected to by the Examiner.</p> <p>10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).</p> <p>11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.</p> <p>12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.</p>								
<b>Priority under 35 U.S.C. §§ 119 and 120</b> <p>13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</p> <p>*See the attached detailed Office action for a list of the certified copies not received.</p>								
<p>14) <input checked="" type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.</p> <p>15) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.</p>								
<b>Attachment(s)</b> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;"><input type="checkbox"/> Notice of References Cited (PTO-892)</td> <td style="width: 33%;"><input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____</td> </tr> <tr> <td><input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</td> <td><input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</td> </tr> <tr> <td><input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____</td> <td><input type="checkbox"/> Other: _____</td> </tr> </table>			<input type="checkbox"/> Notice of References Cited (PTO-892)	<input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____	<input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	<input type="checkbox"/> Notice of Informal Patent Application (PTO-152)	<input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____	<input type="checkbox"/> Other: _____
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<input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____	<input type="checkbox"/> Other: _____							

## DETAILED ACTION

**Please note:** The number of Art Unit 1627 has been changed to 1639. Please direct all correspondence for this case to **Art Unit 1639**.

1. The Response filed on February 14, 2003 (Paper No. 31) is acknowledged. No claims were amended, added or cancelled. Therefore, claims 1, 3 and 5-20 are pending.
2. Claims 11-18 and 20 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to non-elected species, there being no allowable generic claim. Election was made without traverse in Paper No. 9.
3. Therefore, claims 1, 3, 5-10 and 19 remain under examination.

### *Status of Rejections*

4. The previous rejection under 35 U.S.C. 103 is maintained. Applicant's arguments are addressed in paragraphs 8-18. Please especially note paragraphs 9 & 14-16.

### *Claim Rejections - 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3, 5-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasila et al (US 5,972,595; of record) in view of Brown et al (High Throughput Screening, 1997).

Kasila et al teach a method for measuring enzyme activity using a solid support coated with a hydrophobic layer (see column 2, lines 10-23). Specifically, the solid supports are 96-well Flashplates<sup>TM</sup> (which are a scintillating material; see definition, column 2, lines 48-50) coated with an artificial lipid layer in various ways (see, for example, column 4, lines 25-38 and column 5, line 63 through column 6, line 22). Enzyme substrates are bound via hydrophobic interactions within the lipid layer (column 3, lines 26-39). The biochemical transformation of the bound substrate causes a cleavage of a portion of the molecule, thus rendering it hydrophilic (see patented claims, especially claim 1). The hydrophilic portion is washed away, thus reducing the level of scintillation (see, for example, column 5, lines 36-60). The

assay of Kasila et al can be used to study various enzymes and is designed to study them in high-throughput fashion (column 6, lines 24-60).

Kasila et al lacks the specific teaching of where the “reaction product of the chemical or biochemical transformation binds to the scintillating material” to produce a signal above background. The reference teaches the opposite scenario (reaction product is washed away, thus reducing the level of scintillation); however, the reference teaches that a variety of enzyme assays can be conducted using their methodology with different method steps, enzymes, labels and solid supports (see column 3, line 25 – column 4, line 19). For example, Kasila et al teach that the “enzyme activity can be measured by detecting the reporter label fragments in the aqueous material” (column 4, lines 8-9). Importantly, Kasila et al teach “the use of a substrate that allows the study of enzyme activity in samples without the need to extract the reaction products” and that “[w]ith appropriate substrate design” their invention “can be used to study a variety of enzymes...for which the assay methods otherwise require extraction steps” (column 3, lines 10-25). Thus, it is the examiner’s position that Kasila et al teach the general conditions of the instant claims and to modify the teachings of the reference where the “reaction product of the chemical or biochemical transformation binds to the scintillating material” to produce a signal above background would be obvious to one of ordinary skill. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Moreover, the binding of radioactive elements to scintillating material in an enzyme assay was well established in the art at the time of filing. For example, Brown et al teach the advantages of using the microplate surface scintillation effect in general (page 317), and for enzyme assays in particular (Section IV, beginning on page 321). These offer the opportunity to save time and cut costs (see Section VI, Summary, page 327).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Kasila et al where the "reaction product of the chemical or biochemical transformation binds to the scintillating material" to produce a signal above background. The motivation is two-fold: (1) because the general conditions of a claim are disclosed in Kasila, it is not inventive to discover the optimum or workable ranges by routine experimentation (*In re Aller*, cited above); also (2) since the binding of radioactive elements to scintillating material in an enzyme assay was well established in the art at the time of filing (as evidenced by Brown et al), it would have been obvious to one of ordinary skill that this format was a desirable one for enzyme assays. Brown teaches that such assays save time and cut costs (see above). Also, Kasila et al teach that "[w]ith appropriate substrate design" their invention "can be used to study a variety of enzymes...for which the assay methods otherwise require extraction steps" and that the "particular substrate to use is designed or selected for its susceptibility to the action of the enzyme and an appropriate location for the label" (column 3, lines 10-25).

***Response to Arguments***

8. Applicant's arguments filed February 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.
9. After careful consideration of the instant case, it is the examiner's position that the above rejection should be maintained. Although applicant's arguments are valid in part (addressed fully below), the instant claims are lacking limitations that fully express the claimed invention as argued.
10. Applicant discusses the Kasila reference on page 1 of the Response, stating that Kasila lacks the specific teaching of where "the reaction of a product of the chemical or biochemical transformation binds to the scintillating material to produce a signal above background (increased scintillation correlates with the progression of the reaction)". While it is true that Kasila does not specifically teach this, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is elaborated upon in the next paragraph.
11. The instant claim 1 states in step b) that "the scintillating material can be stimulated to scintillate above background by at least one of the adsorbed molecular species" (emphasis added) and goes on in step d) to recite "wherein the reaction product of the chemical or biochemical transformation binds to the scintillating material, and at least one of the reactants of said chemical or biochemical transformation does not bind to the scintillating material".

Thus, the instant claims are not limited to the scenario where the reaction product of the chemical or biochemical transformation binds to the scintillating material *to produce a signal above background* since claim 1 only states “the scintillating material can be stimulated to scintillate above background by at least one of the adsorbed molecular species”. Also, there is absolutely nothing presently in the claims indicating that “increased scintillation correlates with the progression of the reaction” as argued by applicant. Thus, although it is true that Kasila specifically teaches washing the reaction product away, thus reducing the level of scintillation, it is not clear that the instant claims are limited to a scenario where increased scintillation is measured (correlating with the progression of the reaction).

12. Applicant argues on page 2 of the Response that the method of Kasila and Brown would need to be fundamentally changed to result in the method of the claimed invention and that the references “fail to suggest to one of ordinary skill in the art modifications needed to meet all claim limitations”. The examiner respectfully disagrees. Although Kasila specifically teaches washing the reaction product away, thus reducing the level of scintillation, the reference also teaches that a variety of enzyme assays can be conducted using their methodology with different method steps, enzymes, labels and solid supports (see column 3, line 25 – column 4, line 19). For example, Kasila et al teach that the “enzyme activity can be measured by detecting the reporter label fragments in the aqueous material” (column 4, lines 8-9). Importantly, Kasila et al teach “the use of a substrate that allows the study of enzyme activity in samples without the need to extract the reaction products” and that “[w]ith appropriate substrate design” their invention “can be used to study a variety of

enzymes...for which the assay methods otherwise require extraction steps" (column 3, lines 10-25).

13. Also, the examiner pointed to Brown for teachings of the advantages of using the microplate surface scintillation effect in general (page 317), and for enzyme assays in particular (Section IV, beginning on page 321). When one looks to the enzyme assays in Section IV of Brown, it is clear that a variety of formats are taught; see e.g. page 325, 1<sup>st</sup> paragraph, which *describes an assay that shows that "increased scintillation correlates with the progression of the reaction"*.

14. Importantly, the interpretation of the claims in light of the specification should be considered. The instant specification states that a wide variety of formats are contemplated for the interaction of substrate and product, including several examples that would result in decreased scintillation as the reaction progresses (see page 17, lines 1-17). There is at least one assay specifically set forth in the specification that results in decreased scintillation as the reaction progresses, see page 18, lines 9-17, directed to a phosphatase reaction. See also page 16, lines 21-23. However, the instant claims are not limited in any way to a particular reaction, particular surface of the scintillating material or particular "molecular property-based binding interaction". Dependent claims 3 and 9 would cover both assay scenarios where increased or decreased scintillation could be seen.

15. Most importantly, although dependent claim 20 is currently withdrawn from consideration, it should be noted that this claim specifically recites phosphatase catalyzed reactions. As described in paragraph 14 above, these reactions are specifically described in the instant specification to result in decreased scintillation as the reaction progresses, see page 18, lines 9-17.

16. Thus the instant claims do not have the necessary specificity (i.e. do not contain limitations) for the particular reaction, particular surface of the scintillating material and/or particular “molecular property-based binding interaction” and are not limited to scenarios where increased scintillation correlates with the progression of the reaction. In fact, the instant claims appear to encompass scenarios where either increased or decreased scintillation could be seen (see paragraphs 14 & 15 above). As stated in the rejection, since the binding of radioactive elements to scintillating material in an enzyme assay was well established in the art at the time of filing (as evidenced by Brown et al), it would have been obvious to one of ordinary skill that this format was a desirable one for enzyme assays. Brown teaches that such assays save time and cut costs (see rejection). Also, Kasila et al teach that “[w]ith appropriate substrate design” their invention “can be used to study a variety of enzymes...for which the assay methods otherwise require extraction steps” and that the “particular substrate to use is designed or selected for its susceptibility to the action of the enzyme and an appropriate location for the label” (column 3, lines 10-25).

17. Lastly, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Response, page 2, bottom), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The examiner maintains that the combined teachings of the cited references indicate information that was within the level of ordinary skill and render the claimed invention *prima facie* obvious.

18. For these reasons and the reasons of record, the rejection under 35 U.S.C. 103(a) is maintained.

*Status of Claims/Conclusion*

19. No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period,

then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.  
May 14, 2003



MAURIE GARCIA BAKER PH.D  
PRIMARY EXAMINER